Express Mail No.: EL 852 462 036 US   Mailed on: Jun 5, 2001

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UNITED STATES LETTERS PATENT

on

CALORIMETRY AS A ROUTINE DOSIMETER AT AN ELECTRON BEAM PROCESSING FACILITY

Drawings: Three (3) sheets
Docket No. 25141-3160 (ACS 1931)

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CALORIMETRY AS A ROUTINE DOSIMETER AT AN ELECTRON BEAM PROCESSING FACILITY

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of and priority from Provisional Application Ser. No. 60/275,556 filed on March 13, 2001, which is hereby incorporated by reference in its entirety.

FIELD OF INVENTION

The invention relates to the fields of dosimetry and calorimetry, in particular routine dosimetry using calorimetry for the routine monitoring and control of ionizing radiation processing procedures.

BACKGROUND OF THE INVENTION

Radiation processing, the treatment of items with radiation, plays an important role in the production of many products. A radiation process is a method or procedure which uses radiation processing, such as radiation sterilization. Radiation may be used in a radiation process for the sterilization of materials, particularly for medical instruments and accessories, for the pasteurization of food products, and for material processing, such as for inducing or enhancing the polymerization of materials or the introduction of dopants or impurities into substantially pure materials. Electron-beam radiation is a common form of radiation used in radiation processes for sterilization,

pasteurization, and for alteration of the properties of materials.

A radiation dosage is an amount of radiation absorbed by an irradiated item. Dosimetry is the measurement of an amount of radiation.

Measurement, by means of a dosimetry system, and reporting of the amount of radiation absorbed by items to be sterilized or otherwise processed by radiation is an important quality control measure. Reporting requirements in highly regulated industries, such as those typically using radiation processing, are stringent and often require much effort. Calibration of the dosimetry system, comprising comparison of the dosimetry system measured values with those of national standard radiation sources with different control settings, is typically performed before use of a radiation source, and optionally at other times thereafter, to determine whether the dosimetry system is providing accurate radiation dosage measurements. The calibrated dosimetry system is used, if necessary, to adjust the radiation source so that it performs as desired. Quality control measurements may be routine measurements taken infrequently or frequently, and often at regular intervals, to monitor the performance of the radiation processing on an on-going basis. Such quality control measurements of radiation delivery during radiation processing are termed routine dosimetry measurements, and differ from calibration measurements in that calibration measurements are used to assure the accuracy of the dosimetry system, and to verify that dose measurements obtained are valid, while routine dosimetry measurements track the performance of a radiation process during use.

Two general categories of dosimeters exist, reference standard dosimeters and routine dosimeters. The objective of the reference standard dosimeters is to provide a link between national standard dosimetry calibration laboratories and production radiation processing facilities. The key criteria is control and accuracy of measured dose. Practicality is thus not an issue for reference standard dosimeters since their use during calibration of routine dosimeters is infrequent. Routine dosimeters, on the other hand, are used for regular quality control within a radiation processing plant. Practicality is of utmost importance, combined with reasonable accuracy.

The amount of radiation delivered by an electron beam may be measured in a number of ways. For example, the current induced by the passage of radiation past capacitor plates was reported as a measure of the radiation beam dosage by Taumann, U.S. Patent No. 4,427,890, while the current produced in a coaxial sensor placed in an electron beam was reported to be proportional to an electron beam current intercepted by the sensor, and so was said to be useful as a measure of the beam dosage (Fiorito et al., U.S. Patent No. 4,629,975). The current collected by a beam stop was said by Lawrence et al., U.S. Patent No. 5,661,305, to be a useful measure of the absorbed dose in a product irradiated by an electron beam. All patents cited herein, both *supra* and *infra*, are hereby incorporated by reference in their entirety.

A listing of and a discussion of the advantages and disadvantages of various dosimetry methods may be found in Annex C of "Dosimeters, dosimetry

and associated equipment" ANSI/AAMI/ISO 11137-1995 (1995) (referred to herein as "ISO 11137"). For example, calorimetry is listed therein for use as a reference standard dosimeter, while several spectrophotometric methods are listed as examples of routine dosimeters.

One method of detecting and measuring radiation is to measure the optical density of radiation-sensitive films (also known as radiochromic films) exposed to radiation. Commonly, calibration is performed by irradiation of unexposed radiation-sensitive film routine dosimeters together with controlled reference standard dosimeters from national standards laboratories. The results of such film dosimetry are determined by the amount of exposure of the film following irradiation, such as by measuring the optical density of the developed film. Results of the reference standard dosimeters are then correlated with the results of the routine film dosimeters to form calibration curve for the film dosimeters. Film dosimetry is performed for routine dosimetry to confirm that the appropriate amount of radiation is being delivered to the items to be irradiated, and to correct the exposure if it is found to be inaccurate. However, there is a delay in obtaining film dosimetry readings while the film is developed, and film dosimetry is subject to problems of reliability and consistency due to variation between films, variability of film placement on or within the items being irradiated, variability in the time between irradiation and film development, and the effect of temperature, humidity and ultraviolet light levels on the exposure characteristics of the film (see, for example, Table C5, ISO 11137).

The absorption of radiation heats an object that has been irradiated. Calorimetry, which measures heat, may be used as a method of dosimetry by measuring a temperature change in an irradiated item and correlating the radiation dosage absorbed with the temperature change. However, in order to be accurate, these measurements must be made without allowing any significant loss of heat. Radiation processing with gamma radiation, for example, may take several hours. Electron beam sources typically require a shielding maze and multiple passes within the maze, requiring an hour or more for radiation processing. Significant amounts of heat transfer might occur during this time, making calorimetry measurements difficult and inaccurate under these circumstances. Attempts to calibrate an electron beam source radiation by placing a calorimeter on an arm that swings into the path of the electron beam require that radiation processing of other items be stopped, and the system reconfigured for normal operation before radiation processing is able to begin again. However, such a system cannot be used for routine dosimetry measurements because the calorimeter interrupts the normal functioning of the system.

The variability in the measuring tools presently used in routine dosimetry hinders routine measurement of the performance and reliability of radiation sources. However, radiation processing, such as for sterilization, is a heavily audited and critical process in the production of medical implements and medical instrumentation, in food processing, and in the processing of many materials.

The ability to minimize quality control issues related to routine dosimetry would improve present methods and significantly reduce the risk of non-compliance with the strict regulations that are typically applied to radiation processing.

Accordingly, what is required are systems and methods for radiation processing and for routine dosimetry that are not affected by sensor location, variability in sensing elements, and other such problems, and are capable of being used without interference with the normal operation of radiation processing methods.

SUMMARY OF THE INVENTION

The present invention is directed to a method and system for determining a radiation dose for the quality control of a radiation process, and particularly to a method and system for routine dosimetry for the sterilization of medical products.

A system embodying features of the invention, such as a system for routine dosimetry, includes a calorimeter, particularly a thermistor calorimeter, a radiation source, and a calorimetry control system. Such systems are particularly suitable for use in sterilizing medical products.

The calorimeter should have a validated resistance-temperature calibration relationship and a validated temperature-dosage relationship. Irradiation of the calorimeter heats the calorimeter. The temperature of a calorimeter after irradiation is preferably measured before significant heat loss has occurred. In routine dosimetry, calorimeter temperature is measured as soon as possible after irradiation so that only very small amounts of heat are lost.

Preferably, the loss of heat from the calorimeter is a linear function of time after irradiation. In embodiments of the system, the calorimeter is configured to reduce or prevent heat loss, such as by insulation or by maintaining the external temperature near to the temperature of the heated calorimeter..

The radiation source may be a controlled radiation source, and is preferably a high dose-rate radiation source. The high dose-rate radiation source may be an electron radiation source. Radiation doses provided by the radiation sources of the systems of the invention may be between about 0.1 kGy to about 100 kGy. In embodiments, the radiation dose is between about 2 kGy to about 70 kGy, and in still further embodiments, the radiation dose is between about 3 kGy to about 40 kGy.

The calorimetry control system may include a calorimeter controller, which may monitor and/or direct the performance of the system and its components. The calorimeter controller should be an automatic calorimeter controller, and preferably should be a computer-controlled automatic calorimeter controller. In routine dosimetry control the interval between routine dosimetry measurements is constant, unless the target radiation dose has changed, in which case a routine dosimetry measurement is taken regardless of the amount of time that has passed since the previous routine dosimetry measurement. Typically, the interval between dosage determinations is less than about an hour, preferably less than about a half hour.

The systems may further include a conveyor system for effecting relative

motion between a radiation source and items and calorimeters to be irradiated. The conveyor should be effective to move the calorimeter through the path of radiation from the radiation source, preferably within a short time. The conveyor may move the calorimeter along a short, closed-loop route so as to return the calorimeter to and ending position within a short time. In embodiments, the ending position is or is near to the starting position.

In addition, the systems of the invention may further include a robotic arm having a resistance measuring device able to temporarily contact and obtain a resistance measurement from the thermistor calorimeter.

The present invention further provides methods for routinely determining and reporting a radiation dose for quality control of a radiation process, which is particularly suited to routine dosimetry for the sterilization of medical products. Routine dosimetry methods embodying features of the invention include measuring an initial calorimeter temperature, irradiating a calorimeter, and measuring a subsequent calorimeter temperature.

The calorimeter temperature is measured before and after irradiation of the calorimeter by the radiation source, and the radiation dose received by the calorimeter is determined using the calculated temperature difference between the initial temperature and subsequent temperature measurements of the calorimeter, and using the resistance-temperature and temperature-dose calibration relationships in conjunction with the temperature differential. Preferably, the irradiation of the calorimeter is performed in the same manner as

the irradiation of items, such as medical products receiving radiation sterilization, is performed. The dose determination procedure is preferably repeated at an interval, or after a specified number of items has been processed, or by other criteria, determined by the calorimeter controller. The determined dosage may then be reported.

The calorimeter controller may be used to determine and/or control the interval between routine dosimetry measurements. For example, the calorimeter controller may be used to determine whether the dose from the radiation source has been changed, and to maintain the interval between routine dosimetry measurements constant when the radiation dose has not changed. The calorimeter controller may also be programmed to prompt or initiate a calorimeter measurement whenever the radiation dose from the radiation source has changed. In addition, the calorimeter controller may be employed to determine whether the calorimeter has validated resistance-temperature and temperature-dosage relationships, i.e., is a validated calorimeter, may be programmed to accept data only from validated calorimeters, and may manage the printing of a process report.

Thus, a method embodying features of the invention comprises: providing a calorimeter control system and a calorimeter; measuring an initial calorimeter temperature; irradiating the calorimeter with a dose of radiation from a radiation source; measuring a subsequent calorimeter temperature before significant heat loss has occurred; determining the radiation dose using a calculated temperature

difference between the initial temperature and subsequent temperature measurements, and using the resistance-temperature and the temperature-dosage calibration relationships; repeating these procedures at an interval determined by the calorimeter controller; and reporting the radiation dose. In embodiments, the calorimeter is a thermistor calorimeter, preferably a validated thermistor calorimeter having a validated resistance-temperature calibration relationship and a validated temperature-dosage calibration relationship.

Preferably, the calorimeter measurements taken subsequent to irradiation are taken as soon as possible after irradiation so that only small quantities of heat are lost from the calorimeter, or so that the heat loss will be a nearly linear function of time after irradiation. To minimize such heat loss, and so to measure the calorimeter temperature before significant heat loss has occurred, the time the calorimeter temperature is taken after irradiation should be a short time, such as less than about an hour, preferably less than about 30 minutes, and more preferably less than about 15 minutes. Other methods may also be used for minimizing heat loss and insuring that calorimeter measurements may be made before significant heat loss has occurred, such as providing insulation, raising environmental temperature, or other methods.

In embodiments of the routine dosimetry method, the irradiating procedure further comprises movement of a calorimeter by a conveyor along a route. Such a route may be a short, closed-loop route. The calorimeter may be conveyed along a route at a rate effective to return it to its starting position within

a short time, or to an ending position which may be near to the starting position, within a short time. Such a short time may be less then about 30 minutes or, preferably, may be less than about 15 minutes. In embodiments of the methods, calorimeter temperature measurements are taken at locations determined by the conveyor route, typically at locations near to the starting position and/or ending position along the conveyor. In embodiments of the method, the time required to convey a calorimeter along a route between starting and ending positions is substantially the same as the time interval between initial and subsequent calorimeter measurements. Such a time interval is preferably a short time.

In one embodiment, the radiation source is a high dose-rate radiation source, such as an electron radiation source. The radiation dosage output capability of the radiation source should be between about 0.1 kGy to about 100 kGy, preferably between about 2 kGy to about 70 kGy. For sterilizing medical products such as guidewires, catheters, and the like for vascular procedures, suitable dosage rates may range from about 3 kGy to about 40 kGy.

Determining a radiation dose includes contacting the thermistor calorimeter with a measuring device and at least temporarily moving the temperature measuring device while in contact with the thermistor calorimeter to obtain a calorimetry measurement from the calorimeter. The temperature measurement preferably is a resistance measurement.

The invention also provides a routine dosimetry control method for determining at intervals and reporting an acceptable radiation dose in a radiation

process comprising a calorimeter that has a maximum lifetime dose. Such embodiments of the routine dosimetry control methods comprise determining whether a calorimeter is valid and has received less than a maximum lifetime radiation dose. The calorimeter is determined to be a validated calorimeter if it is a valid calorimeter and has received less than a maximum lifetime radiation dose.

The invention yet further provides a method for radiation processing of an item, such as a medical product, comprising processing a calorimeter in a radiation process according to a routine dosimetry method of the invention, and processing an item in the radiation process. Preferably, the calorimeter and the processed items are irradiated in the same manner, preferably by the same radiation source.

In addition to the particular embodiments listed above, it will be understood that other combinations and arrangements of the components and procedures of the systems and methods described may be used in the practice of the invention. All such combinations and arrangements are within the scope of the present invention.

The routine dosimetry systems and methods of the present invention provide benefits that include reduced labor requirements, reduced environmental requirements, and increased consistency and quality of dosimetry results for both processing dosimeters and investigating dosimetry issues. Other dosimetry methods commonly used at present, such as film or other spectrophotometric

methods, have disadvantages such as requiring the calibration of optical equipment and the maintenance of special environments.

Practice of the methods of the present invention are effective to reduce the labor needed to perform a radiation process; for example, an automatic calorimeter controller eliminates the need for a person to read or process dosimeters, improves reliability and repeatability of the processes, thereby reducing stoppages and reducing wastage. Automatic control of a radiation processing system allows for the automatic collection and recording of data for process reports, reducing the costs of compliance with regulatory requirements. Thus, the radiation processing and routine dosimetry as performed in the practice the present invention can be accomplished with fewer resources, with far superior quality and with far less compliance risk than prior methods.

These and other advantages of the invention will become more apparent from the following detailed description of the invention and the accompanying exemplary drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a flow diagram illustrating a routine dosimetry control method embodying features of the invention.

Fig. 2 is a flow diagram illustrating a method of radiation processing comprising a routine dosimetry control method in a radiation sterilization process embodying features of the invention.

Fig. 3 is a plan view of a radiation processing system embodying features of the invention.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides improvements in radiation processing, comprising improvements in methods of measuring radiation in methods and systems for radiation processing. The inventors here disclose novel methods and systems for the use of calorimetry for radiation processing such as radiation sterilization and routine dosimetry in methods and systems for sterilization. The novel methods may be particularly useful as systems and methods for routine dosimetry for sterilizing medical products. The novel methods for routine dosimetry comprise the routine monitoring of the performance of ionizing radiation processing facilities using calorimetry. A preferred embodiment of the method is a method of utilizing calorimetry for routine dosimetry in a radiation process. A radiation process may comprise, for example, a process for radiation sterilization of an item. It should be noted that the terms "process" and "method" as used herein are synonymous.

Thus, the invention provides methods and systems for routine calorimetry measurements for routine dosimetry for quality control of a radiation process. In preferred embodiments, the system has a short, closed-loop route in the shape of a simple oval race track-like processing conveyor and shielding design that accommodates rapid transport between the load and unload areas. In this

manner, irradiated items may be loaded onto the conveyor, receive radiation and arrive at the unload area in a short time. In preferred embodiments, the thermistor calorimeter is provided with adiabatic insulation to retain heat evolved during irradiation. Thus, the systems and methods of the invention make insignificant the loss of the heat generated by the irradiation during these short time periods, so that, where the irradiated item is a calorimeter for routine dosimetry, calorimetry measurements are reliably correlated to the radiation dosage, and corrections for the short periods of time between irradiation and temperature measurement are minimal and easy to predict accurately.

The system and methods comprise a calorimetry controller which determines whether a calorimeter is valid. A valid calorimeter has a valid resistance-temperature relationship and a valid temperature-dose relationship. Valid resistance-temperature and temperature-dose relationships comprise relationships in which a dose determined using the resistance-temperature and temperature-dose relationships and a dose traceable to a dose determined by a national calibration laboratory dose measurement match to within a specified degree. In embodiments of the routine dosimetry control method, the specified degree of match between a dose traceable to a dose determined by a national calibration laboratory dose measurement and the dose determined using the resistance-temperature and temperature-dose relationships is less than about 15 %; in yet further embodiments, the specified degree of match is less than about 5%.

A database of validated calorimeters may be kept, calorimeters identified, as by a bar code or other label or identification, and by scanning the bar code or otherwise identifying a calorimeter, the calorimeter controller may determine whether the calorimeter is valid. Criteria for validity include resistance-temperature and temperature-dose relationships that are within specified ranges, and a cumulative lifetime level of radiation exposure that is less than a maximum lifetime dose. Calibration relationships may be determined by comparing calorimeter dose measurements to dose measurements made under the same conditions using national calibration laboratory dose standards. The National Institute of Standards and Technology (NIST) and the National Products Laboratory (NPL) in the United Kingdom provide such calibration standards.

Calorimetry is an inherently simple, accurate and precise measurement of the change in temperature of an item. Absorption of radiation by an irradiated item results in heating of the item that is correlated to the dose of radiation received by the item. It is possible to measure the heat generated by irradiation, and so to obtain a measure of the amount of radiation received by the irradiated item. In particular, the heating of an item by electron beam irradiation may be measured by a calorimeter to provide a measurement of the dose absorbed by an irradiated item. Thus, calorimetry is suitable for measuring the radiation dose absorbed by an item (see, e.g., Table C1 of ISO 11137, and Table 1, "Standard guide for selection and calibration of dosimetry systems for radiation processing" American Society for Testing and Materials, 1994 publication ASTM E 1261-

1994 "ASTM 1261").

Such radiation-induced heating is a reliable measure of the amount of radiation arriving at the item, being directly caused by the interaction between the impacting radiation and the irradiated object. For this reason, calorimetry is not subject to the kinds of errors that other methods of radiation measurement are subject to, such as variability in sensing elements or in the location of a sensor with relation to the object. In addition, unlike other methods of measuring radiation dosages, variables in the testing environment such as humidity and ultraviolet light level do not affect calorimeters. These benefits are the reason for calorimetry being used as a reference standard dosimetry method (see, e.g., Table 1, ASTM 1261 and C1 of ISO 11137).

Reference is made to Figure 1, wherein an embodiment of the invention, comprising a routine dosimetry control method, is shown in schematic form. It will be appreciated that the method disclosed in Figure 1 comprises one of many embodiments of the invention, and that other embodiments may vary, so that, for example, other procedures may also be included or not every procedure illustrated in the process disclosed in Figure 1 need be performed in the practice of the invention.

The method illustrated in Figure 1 is a routine dosimetry control method comprising a method for measuring a radiation dose from a radiation source, such as a high dose-rate radiation source. A high dose-rate radiation source typically provides radiation at a dose rate of at least 10 Gy/s, typically at dose

rates of about 100 to about 1000 Gy/s, more typically at dose rates of about 250 to about 1000 Gy/s (where "Gy" is a Gray, a radiation dose equivalent to the absorption of 1 joule per kilogram). The radiation source has a target radiation dose rate that is the dose rate desired to be delivered by the radiation source. The target dose rate is typically specified by beam parameters used by a radiation beam controller, such as an electron beam controller. A target dose in a radiation process is the dose that is desired to be delivered to an irradiated item by the beam source. Routine dosimetry measures and records the radiation doses actually delivered by the radiation source providing the routine measurements required in quality control of a radiation process.

The method illustrated in Figure 1 comprises the procedures of irradiating a calorimeter, and measuring heat with the calorimeter effective to provide a measurement of heat evolved from the irradiating procedure. In the practice of this method with a thermistor calorimeter, the procedure of measuring heat comprises taking a resistance measurement and calculating a temperature difference using the calorimeter's Resistance-Temperature (R-T) calibration relationship (a relationship is also termed a curve, so, e.g., this is also termed the R-T calibration curve) to provide a measurement of the heat evolved from the irradiating procedure. By means of the calorimeter's Temperature-Dose (T-D) calibration relationship or curve, the temperature difference and the measurement of the evolved heat derived from it can be used to determine the amount of radiation received by the calorimeter.

The method of Figure 1 is illustrated by means of a flow chart, in which the procedures of the process are represented by a square, a diamond, or a square with one rounded side. Squares represent procedures of the process where the process proceeds directly to the next procedure upon completion of the indicated action; diamonds indicate branch points from which lead alternative paths, so that a decision must be made to determine which of the alternate paths to follow; and a rounded square indicates a halt in the process, where the process waits for a time or only continues to the next procedure upon fulfillment of a criterion. Arrows indicate the temporal direction of the process, with procedures at the arrow head being subsequent to procedures at the tail of the arrow. Thus, in the processes illustrated in Figure 1 and in Figure 2, the direction of an arrow, from tail to arrow head, indicates the sequence of procedures to be taken in the processes illustrated.

The embodiment of the method illustrated in Fig. 1 begins with procedure 1 termed “Calorimeter Process Start” signifying the initiation of the process. Procedure 2, “Prompt Calorimeter,” is a procedure in which the control system prompts the operator that, based on the process criteria, the time has arrived for another routine calorimeter measurement and a calorimeter should be entered into the system (e.g., onto the conveyor system) for processing. In an automatic or partly automatic process, where an operator need not be involved at this procedure, the prompt would consist of an automatic signal, or to automatically beginning a routine dosimetry measurement. Examples of such process criteria

that could trigger the initiation of another routine dosimetry measurement include the passage of a pre-determined interval of time, and a change in the target radiation dose-rate of the radiation source.

Procedure 3, "Identify Calorimeter" comprises a procedure where the individual calorimeter is identified, as, for example, by noting a serial number, or reading a bar code. (The calorimeter may have already been identified prior to procedure 2 if the process had proceeded to procedure 2 from procedure 7.) Procedure 4, "Calorimeter has Valid Cal. Curve?" referring to a calibration curve for the particular calorimeter, comprises a procedure where the identification of the calorimeter is used to check whether that particular calorimeter has been properly calibrated, and whether the calibration of the calorimeter is still valid. The calibration relationship involved at this procedure is typically with regard to the R-T calibration curve and the T-D calibration curve. Thus, a calorimeter passing this procedure has been validated as to its calibration curve. Such a check may be performed by inspection of written calorimeter calibration records, by computer-assisted inspection of digital records, by performance of a calibration, or by other means known in the art. Procedures for calibration of the calorimeter will differ between different types of calorimeters, but are well known to those of ordinary skill in the art. For example, calorimetric methods for dosimetry may be found in "Use of Calorimetric Dosimetry Systems for Electron Beam Dose Measurements and Dosimeter Calibrations" (<u>Annual Book of ASTM Standards</u>, publication E 1631-96, American Society for Testing and Materials,

West Conshohocken, PA 19428 (1999) "ASTM 1631"). In general a calorimeter calibration procedure comprises a series of measurements taken at different known radiation doses, so that the output of the calorimeter as a function of radiation dose is thereby determined. It will be understood by those of ordinary skill in the art that the criteria for validity of the calibration may vary, and may depend on the type, sensitivity, and stability of the calorimeter, any regulatory requirements that may apply, and other factors known to those of ordinary skill in the art. Procedure 4 is a branch point in the process, where the next procedure to be taken is determined by the decision made during procedure 4. In the instance where the calorimeter does not have a valid calibration curve, the next procedure in the process after procedure 4 is procedure 7, "Record Cal. Invalid." If, however, the calorimeter does have a valid calibration curve, the next procedure in the process is procedure 5.

Procedure 5, "Calorimeter < max dose?" again uses the identification of the calorimeter from procedure 3 to allow inspection of calorimeter records to determine whether the cumulative radiation received by a particular calorimeter during its operational lifetime is below or is at or has exceeded its allowed cumulative radiation dose. Thus, a calorimeter passing this procedure has been validated as to its lifetime maximum dose. The actual value of a maximum dosage for a calorimeter will vary, and may depend upon the type of calorimeter (including depending on the materials used, the design and the method of manufacture of the calorimeter), the sensitivity of measurement that is required,

regulatory requirements that may apply, and other factors known to those of ordinary skill in the art. Typically, a maximum lifetime dose will be in the range of about 1 to about 5 megaGray (MGy) of radiation. Information regarding such factors may be found in ASTM 1631.

Thus, procedure 5 is also a branch point; if the calorimeter has reached its maximum dose, procedure 5 leads to procedure 6; if, however, the cumulative radiation dose absorbed by the calorimeter is below the maximum dose, then the process proceeds to procedure 8. Procedure 6, "Calibration Due" indicates that, where a calorimeter has reached its maximum dose, the calorimeter must be re-calibrated (to verify its continued accurate performance) before using it to monitor a radiation dose in a sterilization procedure, or must be replaced by another calorimeter that has not received an excessive amount of radiation. Following procedure 6, if the maximum dose has been exceeded, or following procedure 4 if the calibration curve was not valid for any reason, the process goes to procedure 7, where the calorimeter is marked or listed in a record book, or listed in an electronic record such as a database, or otherwise identified as not available for further use in a calorimeter process. After procedure 7, the process then returns to procedure 2. In this case, the calorimeter arriving at procedure 2 is one in need of re-calibration, and procedure 2 then comprises a calibration procedure, including appropriate updating of records regarding the calorimeter. From this point, the process continues on again to procedure 3. If, however, the calorimeter fails the recalibration at procedure 2, or is otherwise determined to

be unusable at procedure 2, instead of proceeding to procedure 3 the process proceeds to procedure 19 ("End if not calibratable") with the rejection of the calorimeter and ending of the procedure. The process may be begun again at procedure 1 with a different calorimeter.

Where the calorimeter has a valid calibration curve and has not exceeded its maximum dose, the process proceeds from procedure 5 to procedure 8. Calorimeters passing procedures 4 and 5 may be termed "validated calorimeters." Procedure 8, "Initial Calorimeter Measurement," is a calorimetry measurement taken before irradiation of the calorimeter in order to provide a baseline measurement. At procedure 9, "Record Initial Measurement," the results of the initial calorimetry measurement made at procedure 8 are entered into the recording system, e.g. by hand into a log-book, or by keyboard entry into a computerized record system, or the like. It will be understood by one of ordinary skill in the art that there are many suitable methods for recording the results of a calorimetry measurement, and that any such method may be used in the practice of the invention.

At procedure 10, "Calorimeter Processed Through Beam," the calorimeter is irradiated as it is processed through a radiation beam, such as an electron beam. After irradiation, another calorimeter measurement is taken at procedure 11, "Calorimeter Measurement Following Irradiation," and the results of the measurement are recorded at procedure 12, "Record Measurement After Irradiation."

It is critical that only a short time intervene between the irradiation of the calorimeter at procedure 10 and the calorimetry measurement at procedure 11. During such a short time, the heat loss from the calorimeter is negligible or very small, so that the measurement of the heat evolved during the irradiation procedure is, or is very nearly, an adiabatic measurement. A short time may comprise less than about an hour, or preferably less than about half an hour. In more preferred embodiments, the time between irradiation of the calorimeter and the calorimeter measurement is less than about 15 minutes. In addition, by calibrating the temperature change properties of a particular dosimeter, it is possible to account for the temperature change that may occur during the time between irradiation and the routine dosimetry measurement and so to improve the accuracy of the process.

Providing a short route of travel for the calorimeter as it is conveyed through the path of the radiation beam is effective to provide that there is only a short time between calorimeter irradiation (procedure 10) and calorimetry measurement (procedure 11). For example, a conveyor route comprising a short oval route is effective to provide such a short time. Alternatively, calorimetry measurements may be made with measuring instruments or measuring tools that are able to contact the calorimeter at points near to the radiation beam on the conveyor route. For example, a robotic arm with a means for measuring calorimeter resistance (such as a probe with an electrical contact connected to a resistance meter) capable of contacting the calorimeter by swinging over the

conveyor route and measuring calorimeter resistance as the calorimeter emerges from the radiation beam path is effective to provide that there only be a short time between the irradiation procedure and the measuring procedure.

A calorimeter controller may take into account the change in temperature that occurs in the time between irradiation of the calorimeter at procedure 10 and the calorimetry measurement at procedure 11. Measurements have shown that this change in temperature is linear for up to an hour after irradiation. In embodiments of the invention, the calorimeter controller uses the known relationship between temperature and time after irradiation for an identified calorimeter to calculate the temperature at the time of irradiation from the measured temperature at a known time after irradiation, and thereby obtain a calculated dose that is more accurate than one not taking this change in temperature over time into account.

Following these measurements, a branch point is reached at procedure 13 "Dose Measurement Acceptable?" and a decision is made based on the amount of radiation received by the dosimeter. The amount of radiation that constitutes an acceptable dose is a parameter of the process that will be determined before the process begins, and will vary with the particulars of the items to be irradiated, regulatory requirements, and other particulars. The dosimeter is a calorimeter, and the radiation dose absorbed by the calorimeter may be calculated by subtracting the temperature measured at procedure 8 from the temperature measured at procedure 11 to calculate the change in

temperature induced by the irradiation procedure and this change in temperature is used to calculate the amount of radiation by means of the calorimeter's calibration curve. Where the calorimeter is a thermistor calorimeter, the temperature measurement comprises a resistance measurement. If the radiation dose is acceptable, then the radiation dose is entered into the records at procedure 14 "Note Acceptable Dose" by any suitable method, as discussed above, and then the process may continue or end at procedure 15, labeled "Return or End." Where the process continues, the procedure following procedure 15 is procedure 1; where the process ends, procedure 15 is the last procedure in the process.

If the radiation dose absorbed at procedure 10 is not acceptable, then the procedure 16, "Notify Operator" will follow procedure 13, where the operator of the process will be notified so that corrective action may be taken to bring the system and process into conformance with its desired performance. Following procedure 16 is procedure 17, "Note Unacceptable Dose," which provides that the records of the process include a notice that the radiation dose was not acceptable, followed by procedure 18, "Stop Further Processing Until Issue Resolved" which insures that no further poorly-processed items result from the process, and that the problem is dealt with expeditiously. After procedure 18 the procedure proceeds to procedure 15 "Return or End" where the next procedure is procedure 1 if the problem that caused the branch from procedure 13 to procedure 16 has been rectified, or the process ends if there has been no

rectification of the problem.

The methods of the invention further provide an irradiation method for irradiating an item comprising the procedures of irradiating a calorimeter, measuring heat with the calorimeter effective to provide a measurement of heat evolved from said irradiation procedure, calculating a change in temperature from said measurement, calculating a radiation dose using the calculated change in temperature, and irradiating an item.

The method of the invention illustrated in Figure 2 is a method of radiation processing. This method, shown in schematic form, comprises an embodiment of the invention wherein the radiation processing comprises radiation sterilization of items in need of sterilization. It will be appreciated that the method disclosed in Figure 2 is one embodiment of the invention, that other procedures may also be included, and that not every procedure illustrated in the process disclosed in Figure 2 need be performed in the practice of the invention.

A calorimeter process comprises a process wherein a calorimeter is used to measure a radiation dose as illustrated in Fig. 1. The calorimeter process referred to in Figure 2, by, e.g., the boxes 26, 32, 34, and 36 labeled "Calorimeter Process," may be a calorimeter process as illustrated in Figure 1, procedure 13, or other such routine dosimetry control process of the invention disclosed herein where a calorimeter is used to measure a radiation dose.

The sterilization method of Figure 2 is initiated at procedure 21, "Start," and proceeds to procedure 22 "Item Logged In" where identifying indicia about

items subject to the process are recorded. It will be understood that such recordation can be performed by hand, mechanically, as by, e.g., a printer, electronically, as by a bar-code reader or magnetic device, or by other suitable means known in the art, either automatically or under the control of a human operator. At procedure 23, "Item in presterile staging," an item to be sterilized is readied for sorting and for loading onto a conveyor for transport during a sterilization process. Following procedure 23, the item proceeds to procedure 24, "Item sorted by processing parameters," where the item may be grouped with other items which are desired to receive the same treatment. At the next procedure, procedure 25, labeled "Parameters Entered," the proper treatment parameters are applied to the electron beam source and conveyor mechanism to provide the desired radiation treatment. The entry of parameters may be done manually by an operator, manually or automatically by means of a computer, by a scanner and bar-code system, or by other suitable means known in the art. Then, at procedure 26, labeled "Calorimeter Process," in a routine dosimetry control process of the invention, e.g., a process like the one illustrated in Figure 1, a calorimeter is subjected to the radiation treatment that is also to be given to the items in need of radiation treatment. As will be appreciated from inspection of Figure 1, if the calorimeter process of procedure 26 results in an unacceptable dose, as determined by, for example, a procedure as in procedure 13 of Figure 1, then the process of Figure 2 halts until the issue has been resolved. Appropriate action may be taken in order to achieve a successful calorimeter

process. For example, where the performance of a calorimeter process is initially unacceptable, achievement of a successful calorimeter process may require readjustment of the radiation source, e.g., readjustment of an electron beam. Indeed, after procedures 1-5 of Fig. 1, it is anticipated that all calorimeter measurements taken at procedure 13 of Fig. 1 (corresponding to procedures 26, 32, 34 and 36 of Fig. 2) are valid measurements indicating quality concerns related to the radiation source. Only in the scenario of a malfunction during procedures 1-5 of Fig. 1 would an unacceptable calorimeter at procedure 13 of Fig. 1 (procedures 26, 32, 34 and 36 of Fig. 2) lead to the potential for the recalibration of a calorimeter that had an invalid calibration curve, or the replacement of an unacceptable calorimeter (e.g., one that had received an excessive amount of radiation) with another calorimeter that is acceptable.

Upon successful completion of a calorimeter process 26 in Fig. 2, items to be processed receive their radiation processing, as indicated by procedure 27 "Lot processed" where the lot may comprise one or a plurality of items desired to receive radiation processing.

Following the radiation treatment of the items in procedure 27, it is determined whether there remain more items to process, as indicated by the diamond 28, labeled "More items to process?" In the event that there are no more items to be processed, then a further calorimeter process, procedure 36, is performed. Following this, at procedure 37, a record of the process is printed, as may be called, for example, a process report or an E-Beam History Report

(EHR), and the sterilization method ends at procedure 38. The procedure of generating a process report can be performed by hand, mechanically, as by, e.g., a printer, electronically, as by a computer, or by other suitable means known in the art, either automatically or under the control of a human operator. The process report may be printed, or displayed and stored electronically or magnetically. The calorimeter process 36 provides for verification of the radiation parameters after the items have received their radiation treatment, so that the radiation treatment is measured before (procedure 26) and after (procedure 36) the items to be sterilized are submitted to the radiation sterilization procedure.

In the event that more items remain to be treated after procedure 27, then the result of the determination of procedure 28 will be that there are more items to be processed; in that case, the process proceeds to procedure 29, "Load next lot," in which procedure the processed items are unloaded and the next lot of items to receive radiation sterilization treatment are loaded onto the conveyor. Then, at procedure 30, labeled "Next lot same parameters?," it is determined whether the radiation treatment parameters for this next lot of items is the same as the radiation treatment parameters for the previous lot. The proper parameters for radiation sterilization and for other radiation processing procedures will vary with the items to be sterilized or processed, the applicable regulatory requirements, and other factors known to one of ordinary skill in the art. If the parameters for the next lot are the same as for the preceding lot, then

no change in the radiation treatment parameters is necessary, and the process proceeds to procedure 31, ">1 hour since last calorimeter?", where it is determined whether the time since the last calorimeter process is greater than one hour or not. If a calorimeter process was performed within the last hour, no additional calorimeter process will be performed at this time, but instead the process returns to procedure 27, "Lot Processed" and the next lot of items receives radiation treatment. If, however, more than one hour has elapsed since the most recent calorimeter process, whether at procedure 26, 32, 34, or 36, then another calorimeter process is performed, at procedure 32, allowing verification that the radiation treatment is still performing within its specified parameters. Following procedure 32, a record of the calorimeter process is printed at procedure 33, labeled "Print Record." The record produced at procedure 33 provides a record of the monitoring procedure 32. After procedure 33, the next procedure is procedure 27 where the next lot of items receive their radiation treatment. It will be understood that requiring routine dosimetry if more than one hour has elapsed since the previous routine dosimetry control process (e.g., a calorimeter process as illustrated in Fig. 1) is one method of the invention, but that providing for routine dosimetry control processes at other time periods, greater than one hour, or less than one hour, or at irregular time periods, are all also within the teaching of the present invention. Thus, in a preferred embodiment, items may be processed for a time, and then a calibration procedure, as in a routine dosimetry control process of the invention, may be

performed before processing further items. Such repeated routine dosimetry control processes as part of a radiation process, such as a method for sterilization, provide for routine monitoring and verification of radiation process procedures, and so aid in their performance and allow for their ready verification and documentation. As mentioned above with regard to procedure 26, and as is the case for each calorimeter process 26, 32, 34 and 36, in the event that the calorimeter process 32 determines that the calorimeter has exceeded its maximum dose, or has an invalid calibration curve, or is otherwise unfit for use for any reason, a different calorimeter may be put into place and subjected to the calorimeter process, or, the process may halt until it may be properly performed.

If, at procedure 30, it is determined that the next lot is not to receive the same parameters as the previous lot, then from procedure 30 the process proceeds to the calorimeter process at procedure 34, providing a calorimeter process that monitors system performance after completion of the radiation treatment analogous to the calorimeter process at procedure 32. Thus, for example, when the radiation beam parameters are changed to provide for a different target radiation dose, a routine dosimetry measurement will be made regardless of the interval of time elapsed since the previous routine dosimetry measurement. The results of the calorimeter process 34 are recorded, e.g., saved in a process report such as an E-beam History Report, at procedure 35, labeled "Print Record." It will be understood that display of an electronically or magnetically generated or stored record is included in the term "print."

The process returns then to procedure 25, where the new parameters are applied, and the performance of the system with the new parameters is monitored in the calorimeter process at procedure 26. The next lot of items then receives its radiation treatment at procedure 27 as the process continues as described above.

The radiation sterilization method illustrated in Figure 2 is an example of one particular type of radiation process suitable for the practice of the invention. Thus, the sterilization method illustrated in Figure 2 provides an example of an embodiment of the invention wherein the routine dosimetry control methods of the invention, such as illustrated in Fig. 1, are used to improve quality control in a method of radiation processing of items. It will be understood that methods may vary in the practice of the invention, and that the order of the procedures, the intervals between calorimeter processes, whether or not, and the method, frequency, and types of records maintained regarding the process, and other particulars of the method may differ while still being within the scope of the present invention.

Reference is also made to Figure 3, which illustrates a radiation processing system 40 embodying features of the invention. Radiation processing system 40 comprises a radiation source 42 effective to emit a radiation beam 44 along a radiation beam path 46 that crosses conveyor 48 that follows a short oval route in this illustration.

The system further comprises a conveyor 48, here shown as following a

short oval course, suitable for carrying an item 50 and a calorimeter 52. The calorimeter 52 is suitable for use as a dosimeter. The item and the calorimeter may be loaded onto the conveyor 48 at the load area 54 and may be unloaded, for example, after processing, at area 56. Conveyor 48 is effective to carry item 50 and calorimeter 52 through radiation beam 44 across the radiation beam path 46. Radiation beam 44 thus contacts item 50 and calorimeter 52, effective to irradiate the item 50 and the calorimeter 52.

A calorimeter measurement may be taken at measuring station 58, information being carried to controller 60 by communication line 62. The short oval route shown is effective to provide that a calorimeter measurement may be made within a short time after irradiation. The controller may comprise a signaling mechanism effective to signal whether a calorimeter measurement has been made, and whether the measurement is within prescribed specifications. Such a signaling mechanism may comprise a mechanical signal mechanism (such as a flag or other indicator), an audible signal (such as a bell or other sounding device), a visual signal (such as a light) or, preferably, an electronic signal (such as an analog or digital signal capable of being read and/or recorded by a computer system). In embodiments of the invention, measuring station 58 comprises a location where a calorimetry measurement is taken. Measuring station 58 may comprise a location where an operator performs a calorimeter measurement, e.g. by using a resistance meter to measure calorimeter resistance. Alternatively, measuring station 58 comprises an automatic

measuring system, such as, for example, a robotic arm effective to move near to or onto the conveyor route and to contact a calorimeter to make a calorimetry measurement, as by measuring calorimeter resistance. In a most preferred embodiment, radiation processing system 40 is a radiation sterilization system. In preferred embodiments, the measurement is able to be automatically recorded or entered into an electronic record of the process, such as into a computer system configured to record the measurements.

In preferred embodiments of the system, radiation source 42 is a high dose-rate radiation source such as an electron beam source. Irradiation causes heat to evolve in the item and in the calorimeter, the amount of heat evolution being proportional to the dose of the irradiation provided by radiation beam 44. A calorimetry measurement by calorimeter 52, such as one made at measurement station 58, is effective to allow calculation of a temperature change caused by irradiation; such a calculated value for a temperature change is effective to allow calculation of a radiation dosage received by the calorimeter 52, from radiation beam 44, that would produce such a temperature change. Thus, the radiation processing system illustrated in Figure 3, which is most preferably a radiation sterilization system, is effective to provide a routine dosimetry measurement for monitoring a radiation process and for use in a sterilization method. In preferred embodiments, controller 60 comprises a device configured to perform the procedures of a routine dosimetry control method, such as a routine dosimetry control method as illustrated in Fig. 1.

Calorimeter controller 60 is in communication with radiation source 42, which may be a controlled radiation source, via communication line 64. Communication line 64 is effective to allow calorimeter controller 60 to monitor radiation source 42, so that, for example, calorimeter controller 60 is able detect when radiation beam parameters change (beam parameters include, e.g., the target radiation dose, that is, the desired dose of radiation to be delivered). Calorimeter controller 60 is able to detect radiation beam parameters via communication line 64 for inclusion in the process reports generated by the routine dosimetry control methods and routine dosimetry methods of the invention.

Calorimeters measure temperature change in a variety of ways, any of which is suitable for use in the present invention. Thermistor calorimeters utilize the well-known thermal-response properties of materials whose electrical resistance changes with changes in temperature.

In the most preferred embodiments of the invention, the calorimeter is a thermistor calorimeter, and the procedure of measuring heat with calorimeter comprises a resistance measurement. Thus, as illustrated in Figure 3, in a most preferred embodiment of the invention, the calorimeter 52 is a thermistor calorimeter and heat is measured by calorimeter 52 by means of a resistance measurement. In most preferred embodiments, the controller 60 comprises a device configured to perform the procedures of a routine dosimetry control process.

Temperature values may be calculated from thermistor resistance measurements by use of empirical mathematical relationships between thermistor temperature and thermistor resistance. The change in resistance with temperature may be a linear function of temperature, as is common with thermistors of the PTC type (where increasing temperature increases thermistor resistance), or it may be a non-linear function, as is common with thermistors of the NTC type (where increasing temperature leads to decreasing thermistor resistance). The relationship between resistance and temperature of a particular thermistor type is known in the art, as may be found, for example, in tables in the CRC Catalog of Chemistry and Physics and the CRC Handbook of Material Science (Chemical Rubber Company, Cleveland, OH) and other standard references.

In addition, the temperature response characteristics of a type of thermistor or of an individual thermistor may be measured in a calibration procedure carried out by the manufacturer, supplier, or user of the thermistor. Such calibration procedures comprise heating or cooling the thermistor to known temperatures, and measuring the thermistor resistance at known temperatures. Temperature may be measured by methods known in the art, for example, by a thermometer, and resistance may be measured by methods known in the art, for example, by an ohmmeter. Resistance-Temperature calibration curves (R-T calibration curves), which are graphs of thermistor resistance versus temperature, are commonly made from such calibration procedures, and are

typically supplied with each thermistor provided by commercial suppliers. (Note that the R-T calibration curves are to be distinguished from the previously-mentioned Temperature-Dose (T-D) calibration curves.) Preferred thermistor temperature readings are obtained when the R-T calibration curve is made from calibration measurements that bracket the desired operating temperature range. Thus, where a thermistor is to be used for temperature measurements near 50 °C, thermistor calibration measurements should be made at temperatures both below and above 50 °C as well as near to 50 °C, e.g., at 25 °C, at 50 °C, and at 75 °C.

The relationship between thermistor temperature and thermistor resistance may be found by fitting a polynomial to resistance measurements obtained at various temperatures. The relationship of thermistor resistance to temperature is discussed in detail in "The exactness of fit of resistance-temperature data of thermistors with third degree polynomials" by M. Sapoff et al., in <u>Temperature Its Measurement and Control in Science and Industry</u> Vol. 5, pages 881-882, ed. J. Schooley, American Institute of Physics, New York, NY (1982). In general, the relationship between temperature and thermistor resistance may be given by polynomials of degree N as:

Equation 1 $$1/T = C_0 + C_1 (\ln R) + C_2 (\ln R)^2 + C_3 (\ln R)^3 + \ldots + C_N (\ln R)^N$$

Equation 2 $$\ln R = A_1 + A_2 / T + C_3 /T^2 + A_3 /T^3 + \ldots + A_N /T^N$$

In most cases, N need be no greater than 3. In addition, it is often the

case that one may dispense with the second-degree term in such polynomials without greatly affecting the goodness-of-fit of the theoretical curve to the empirical data. For this reason, as discussed in Sapoff et al., a commonly used empirical mathematical relationship between thermistor temperature and thermistor resistance is the Steinhart-Hart equation, which generally lacks a second-degree term. The Steinhart-Hart equation, or variations of it, may be used to create a calibration relationship and calibration curve for a thermistor where the resistance of the thermistor is known at three different temperatures. A form of the Steinhart-Hart equation relating temperature to resistance that is useful for such calibration relationships is

Equation 3 $$1/T = C_1 + C_2 \times (\ln R) + C_3 \times (\ln R)^3$$

where T is temperature in degrees Kelvin, C_1, C_2, C_3 are constants to be determined by the calibration relationship, and R is the measured resistance at temperature T. If a lesser degree of accuracy is required, then the above equation may be used without the last term, $C_3 \times (\ln R)^3$ to make for a simpler calculation. This reduced equation with only two constants is

Equation 4 $$1/T = C_4 + C_5 \times (\ln R).$$

Resistance measurements made at different known temperatures may be used in the above equation to calculate the constants. Since there are three unknown constants in the Steinhart-Hart equation, Equation 1, three resistance measurements at three known temperatures are sufficient to provide for three equations to solve for the three unknowns C_1, C_2, and C_3. Where lesser

accuracy is required, and the third term is dropped as in Equation 2, two measurements to provide two equations will be sufficient to solve for the two unknowns C_4 and C_5 of the reduced equation. Sapoff et al. provide more detail regarding the use of the Steinhart-Hart equation. In addition, monographs and computer programs are available to aid in such calculations. For example, the articles entitled "Negative Co-efficient Thermistors," Articles I-IV, from Sensors, Vol. 14, by G. Lavenuta, 1997 (Article I, Vol. 14(5) pages 46, 48, 50, 52, 54-55; Article II, Vol. 14(6) pages 47-49; Article III, Vol. 14(7) pages 17-18, 20; Article IV, Vol. 14(8) pages 54-56) provide graphs and information regarding thermistor properties. BASIC programs for the solution of these equations are available from ILX Lightwave (Bozeman, MT) in their application note #4, which may be found at http://www.ilxlightwave.com/library/appnotes/04/no4i.htm or otherwise obtained from ILX Lightwave.

As discussed in Sapoff et al., such polynomials may be valid over a relevant temperature range. Thus, from equations 1 and 2, for an appropriate temperature range, simple equations relating resistance and temperature may be given by

Equation 5 $\quad 1/T = C_6 + C_7 \times (\ln R)$.

Equation 6 $\quad \ln R = C_8 + C_9 / T$.

In terms of temperature T in degrees Celsius, the relationship may be written:

Equation 7 $\quad T = B/(\ln R + A) - T_k$

where A, B and T_k are empirical constants supplied by the manufacturer with each calorimeter.

The methods of the invention comprise irradiation of a dosimeter, such as a calorimeter, and the systems of the invention comprise a source of radiation effective to emit radiation. In a preferred embodiment, the source of radiation is a high dose-rate radiation source such as an electron radiation source.

The amount of radiation delivered to an item, that is, the radiation dose, is determined by several factors including the intensity of the radiation source, the duration of the irradiation, the distance between the radiation source and the item irradiated, and the orientation of the item with respect to the radiation pathway. Radiation dosage is commonly measured in Gray units, where 1 Gray is equivalent to the absorption of 1 joule per kilogram. Thus 1,000 Gray units, or 1 kGy, represent the absorption of 1000 joules per kg by an irradiated object. In a preferred embodiment of the invention, the electron radiation provides a dose of between about 0.1 kGy to about 100 kGy. In a more preferred embodiment, the electron radiation provides a dose of between about 2 kGy to about 70 kGy. In a most preferred embodiment, the electron radiation provides a dose of between about 3 kGy to about 40 kGy.

The invention provides a system for sterilization and a system for routine dosimetry. The systems comprise a radiation source, a radiation path along which radiation is emitted by the source, and a calorimeter. In preferred embodiments, the calorimeter is suitable for placement in the radiation path

effective to receive radiation from the radiation source. In more preferred embodiments, the calorimeter comprises a thermistor calorimeter.

In a preferred embodiment of the systems of the invention, the radiation source is a high dose-rate radiation source such as an electron beam source and the radiation emitted is an electron beam. In further preferred embodiments of the system, the electron beam is effective to provide a radiation dose of between about 0.1 kGy to about 100 kGy. In more preferred embodiments of the system, the electron beam is effective to provide a radiation dose of between about 2 kGy to about 70 kGy. In most preferred embodiments of the system, the electron beam is effective to provide a radiation dose of between about 3 kGy to about 40 kGy.

In a further embodiment, the systems further comprise a conveyor effective to move the calorimeter. In preferred embodiments, the conveyor is effective to move the calorimeter quickly between the point of irradiation and the point of testing. In most preferred embodiments, the conveyor follows a short, closed-loop route, such as a short oval shaped route, effective to move the calorimeter quickly between the point of irradiation and the point of testing.

In a preferred embodiment, a method is provided for irradiating an item by a radiation source, measuring heat evolved from irradiation, comprising the procedures of irradiating a calorimeter, measuring heat with the calorimeter effective to provide a measurement of heat evolved from the irradiating procedure, calculating a change in temperature, and calculating a radiation dose

using the calculated change in temperature. The calculated change in temperature may be made using the measurement of heat evolved from the irradiating procedure, among other factors. Such other factors may comprise other related measurements and parameters, including but not limited to an initial temperature, performance parameters of the calorimeter, and time after irradiation.

In preferred embodiments of the invention, the irradiation procedure comprises irradiation of an item or a calorimeter where the item or calorimeter is carried on a conveyor to contact a beam of radiation. As illustrated in Figure 3, the irradiation procedure comprises placement of an object to be irradiated, which may be an item 50 or a calorimeter 52, on a conveyor 48 upon which the object is carried into the beam path 46 where it is contacted by beam 44 and thereby irradiated.

In the most preferred embodiments of the methods, the irradiation of a calorimeter is performed in the same manner as the irradiation of an item undergoing a radiation process. It is most preferred that the radiation source is a high dose-rate radiation source. In most preferred embodiments, the radiation is electron radiation. As illustrated in Figure 3 both item 50 and calorimeter 52 are carried by conveyor 48 through beam 44, along the same route, the route of conveyor 48. The irradiation of calorimeter 52 is thus performed in the same manner as the irradiation of item 50 undergoing the radiation process illustrated in Figure 3. In such an embodiment, the calorimetry process is a part of the

overall irradiation process, which need not be stopped or altered to accommodate the calorimeter. Such irradiation may be by any suitable method know in the art.

Any conveyor that is effective to carry an object to or within the radiation beam pathway is suitable for the practice of the invention. Thus, straight, angled, and curved conveyors may be used in the practice of the invention. Conveyors may comprise chain conveyors, linked pallets, conveyor belts, overhead suspension systems, railway systems including monorail systems, and other conveyors known to the art. Motive force for transporting objects by conveyor may be of any suitable kind, including mechanical, hydraulic, electrical, or gravitational motive force. A preferred conveyor is a conveyor that follows a short closed-loop route. A short, closed-loop route such as an oval-shaped route is preferred because it shortens the time needed to provide the objects with a desired radiation dosage.

In addition, a short, closed-loop route such as an oval-shaped track conveyor design is advantageous because such a design minimizes the amount of time between the loading an item for irradiation, and the ultimate unloading of the item following irradiation. Benefits of this type of system include the ability to place items in multiply-stacked layers and the ability to place items in a favorable orientation with respect to the radiation path for the most efficient use of the emitted radiation. Thus the use of a short, closed-loop route such as an oval-shaped track facilitates the practice of the present invention.

Another application of the invention is the use of robotic arms that provide for the testing of the calorimeter within the radiation vault of a radiation processing facility that used a longer conveyor path. Such robotic testing would provide for the quick testing of the calorimeter after irradiation.

Another advantage of the present invention is the simplicity of the method. The routine dosimetry measurements may be collected by standard production operators with no special technical skills and with no special robotic arms within the radiation vault. Automated sensors on the calorimeter, however, may simplify the process. For example, an automated sensor that contacts a sensing lead upon entry to, and exit from, the radiation beam pathway provides automatic calorimetry measurements suitable for the practice of the invention. Thus, the routine dosimetry measurements of the invention do not require inordinate interruption of radiation processing, which is preferably radiation sterilization, and are easy to obtain in the normal course of such processing.

Prior methods required placement of dosimeter film, or other dosimeters, before and after designated items are irradiated in an electron beam facility. In the practice of the present method, radiosensitive films are not used, and routine dosimetry is accomplished by the introduction of a calorimeter, such as a thermistor calorimeter, into the radiation processing facility at intervals. These intervals may be regular intervals, as taught in the method illustrated in Figure 2 where the calibration process is performed at least about once every hour. Alternatively, the intervals may be irregular, or random in time, or may follow a

complicated pattern of time intervals. As taught in the methods of the present invention, the calorimeter is processed in the same manner as are the items being irradiated by the irradiation process.

Thermistor calorimetry data comprise resistance measurements. Such measurements may be used in the determination of the radiation dose absorbed per pass of the calorimeter through the radiation beam. The radiation dose may be determined by calculating the dose using the measured thermistor resistances. The raw resistance data obtained from a thermistor calorimeter may be entered into a spreadsheet for use in performing two calculations. It will be understood that any method of performing such calculations, whether by hand, hand calculator, spreadsheet, programmable computer, dedicated computational circuitry, or other methods, is suitable for the calculation of radiation dose per pass of the calorimeter through the radiation beam.

The first calculation comprises the translation of resistance data to temperature data, and then calculation of the change in temperature resulting from irradiation (calculated by subtracting the calculated temperature measured before irradiation from the calculated temperature measured and after the irradiation process). The translation of resistance data into temperature data is performed by applying a known, calibrated relationship between resistance and temperature for the calorimetry system being used (e.g., the resistance versus temperature relationship of a specific thermistor as in Equation 1 or Equation 2).

The second calculation is performed by translating the change in

temperature into a radiation dose. This is done by means of a known, calibrated relationship (e.g., a National Dose Standards Laboratory relationship) between temperature change and radiation dose. For calibration, the radiation dose may be measured, for example, using an alanine reference dosimeter. Alanine dosimeters may be obtained from National Physical Laboratory (NPL, Teddington, Middlesex, UK)). Similarly, radiation dose standards may be available from the National Institute of Standards and Technology (NIST).

The relationship between temperature change and radiation dose may be determined by fitting a theoretical curve, such as a polynomial curve, to empirical data consisting of measured temperature change values resulting from known radiation dosages. Various methods, including use of a calculator, a programmable computer, a spreadsheet program running on a computer, and other methods, are suitable for determining such a relationship. Such a calibration procedure is similar to the one used to calibrate thermistor resistance as a function of temperature; or a vendor may provide the R-T relationship. For example, a spreadsheet program may be used to perform regression analysis fitting of temperature change data versus the radiation dose absorbed. By selecting an N^{th} degree polynomial that fits the data, and using the constants calculated from it, the dose corresponding to any temperature change within the calibration range can be calculated. Commonly, a second degree polynomial will provide a good fit and enable the calculation of a radiation dose from a temperature change. Thus, for example, Equation 8 may be used for such

calculations:

Equation 8 $$Y \text{ (dose kGy)} = A + BX + CX^2$$

where Y is the calculated dose, X is the temperature change, and A, B, and C are constants determined by the calibration relationship.

The result of these calculations is a radiation dose per pass of the calorimeter through the radiation beam, where a pass is one routine exposure of the calorimeter to the radiation beam. For example, where the conveyor carries the calorimeter in a closed loop route which intersects the path of the radiation beam, a pass is one circuit by the calorimeter along the route that results in a routine exposure to the radiation beam. Where the conveyor route is not a closed loop, a pass is a single complete passage of the calorimeter along the route.

Thus, the present invention provides methods and systems of routine dosimetry and calorimetry, and dosimetry methods that allow the accomplishment of radiation sterilization and routine dosimetry by means of calorimetry with fewer resources than previous methods and systems, with far superior quality and with far less compliance risk. The ability to confirm and monitor the reliability of irradiation, such as electron beam irradiation, is greatly enhanced since the variability of the measuring tool is reduced. Sterilization is a heavily audited and critical process. The ability to minimize the everpresent quality issues related to dosimetry and calorimetry can significantly reduce compliance risk and enhance the competitive advantage of electron beam

radiation processing.

EXAMPLE 1

A short, oval-shaped track chain conveyor system was used to irradiate samples (Surebeam®, Titan Scan Corporation, San Diego, CA). The conveyor system and shielding design of the electron beam process accommodates very small intervals between the time the items to be irradiated leave the load area and the time that the items arrive at the unload area after irradiation that is ideal for calorimeters. Typically, less than 5 minutes were needed to move product from the load area through the electron beam and to the unload area. The products were conveyed via chain conveyors that move captive pallets and product fixtures into and out of the electron beam exposure area.

Radiation dose delivered by the electron beam was calibrated using alanine reference dosimeters as standards. Alanine dosimeters were obtained from National Physical Laboratory (NPL, Teddington, Middlesex, UK)) and were processed by NPL following exposure to measure the dosage received and to provide the radiation dosage calibration.

EXAMPLE 2

RISO National lab type calorimeters (RISO National Laboratories, Roskilde, Denmark, serial numbers #1095 and 1096) were validated for use as routine dosimeters for monitoring the performance of an electron beam process

utilizing the short, oval-shaped track conveyor of Example 1 (Surebeam®, Titan Scan Corporation, San Diego, CA). Each calorimeter is a stand-alone device and is ready to be used multiple times. The calorimeters were polystyrene type calorimeters with a Veco 32A180 Thermistor (an NTC type thermistor), comprising a blown polystyrene foam box containing a polystyrene disc within the foam. Polystyrene has excellent radiation compatibility and insulation properties and is an ideal material for the construction of a calorimeter.

In order to determine the radiation dosage received by a thermistor calorimeter, two relationships must be known and calibrated for the calorimeter: 1) the relationship between thermistor resistance and temperature, and 2) the relationship between the radiation dosage received and the resulting temperature change.

The calibration relationship between the thermistor resistance and temperature was provided by the vendor. It was confirmed and calibrated by imposing different temperatures on the thermistor by placing the thermistor in a temperature bath, monitoring the temperature and measuring the resistance at each of several temperatures.

The equation (see equation 7 above)

$$T(C) = B/(\ln R + A) - T_k$$

describes the relationship between resistance of the thermistor and the temperature of the thermistor. Fitted coefficients provided by the vendor for this equation were:

Thermistor	A	B	T_k
1095	5.9708	4586.13	317
1094	5.9978	4590.72	317

The calorimeters were processed with doses ranging from 2 kGy to 70 kGy together with alanine reference dosimeters by National Physical Laboratory (NPL, Teddington, Middlesex, UK). The alanine reference dosimeters were irradiated in a phantom obtained from Riso National Laboratory so that the alanine dosimeters and the thermistor received the same dose. The resistance of the thermistor in the thermistor calorimeter was measured just prior to and just after each irradiation to determine the temperature of the calorimeter and the change in temperature (ΔT) corresponding to each dose. The calorimeter was allowed to cool to room temperature between irradiations. The alanine reference dosimeters were sent back to NPL for evaluation. The relationship between ΔT and the alanine reference dose was fitted with a second order polynomial.

The procedure for using the calorimeters included the following four procedures. First, to insure that the calorimeter was in thermal equilibrium before irradiation, a multimeter was used to measure thermistor resistance; calorimeters were not irradiated until initial resistance readings were stable at ambient temperature. The resistance of #1095 at ambient temperature was 1900±50 kΩ and the resistance of #1096 at ambient temperature was 1870±50 kΩ. The initial resistance value was recorded in an Excel® (MicroSoft, Redmond, WA)

spreadsheet. Second, the calorimeter was placed on a conveyor fixture and sent along the short, oval-shaped track into the electron beam at the desired speed (ranging from about 0.5 to about 8 feet per minute (fpm)). Third, at the unload station of the short, oval-shaped track, immediately following irradiation of the calorimeter, the multimeter was again connected to the thermistor and resistance was measured and entered in to the spreadsheet. Fourth, the calorimeter was allowed to cool (cooling was assisted by a small fan) and was ready for further validation work when the measured resistance had fallen to ambient levels.

The calorimeter was placed on a pallet and processed in the same manner as other items being processed through the electron beam. The processing parameters were a conveyor speed of about 0.5 to 8 feet per minute (fpm) during exposure to the 10 MeV beam at a power of 6 kW, delivering a dose in the range of 5 to 100 kGy.

A Riso-type calorimeter can be processed at predefined intervals, minimally when electron beam parameters are changed. Typically, such intervals can be one per lot of product, or once per every ten pallets of product processed through the electron beam. The interval used in the measurements reported in this example was one hour. Such calorimeter processing at predefined intervals may be performed fewer than one time per hour, and since the calorimeter is less than I foot in width, this represents a loss of raw processing efficiency of ≤ 2 % [≤ (I ft for a calorimeter)/(60 ft of processing per hour)].

Resistance data was collected directly from the calorimeter, immediately before entry of the calorimeter into the electron beam and immediately after irradiation of the calorimeter by the beam.

The RISO calorimeters #1095 and #1096 were irradiated while being conveyed long a short, oval-shaped pathway through an electron beam (Surebeam®, Titan Scan Corporation, San Diego, CA) at several conveyor speeds,.resulting in the delivery of different dosages for the different speeds. In one experiment for each calorimeter, dose attenuators were used for the fastest conveyor speed (8 feet per minute (fpm)) in order to reduce the dosage. The change in temperature was measured for each different radiation dose. These results are shown in Table 1.

TABLE 1

	Alanine	Speed (fpm)	Dose (kGy)	R_0 (kΩ)	R_1 (kΩ)	T_0	T_1	ΔT
1095								
	36-177	8.0 (atten.)	2.2	1969	1924	21.31	21.89	0.58
	36-178	8.0	4.4	2024	1727	20.62	24.61	3.99
	36-179	5.77	6.6	2000	1612	20.92	26.38	5.46
	36-180	3.71	11	1904	1378	22.15	30.46	8031
	36-181	2.14	20	1931	1109	21.79	36.27	14.47
	36-182	1.46	30	1912	866	22.04	43.13	21.09

	36-183	1.25	35.3	1911	765	22.06	46.67	24.61
	36-184	1.11	40	1913	687	22.03	49.80	27.77
	36-185	0.89	50	1999	578	20.93	54.94	34.01
	36-186	0.64	70	1961	383.3	21.41	67.75	46.35
1096								
	36-177	8.0 (atten.)	2.2	1941	1901	21.33	21.85	0.52
	36-178	8.0	4.4	1995	1703	20.65	24.62	3.98
	36-179	5.77	6.6	1968	1579	20.99	26.56	5.57
	36-180	3.71	11	1891	1360	21.98	30.44	8.46
	36-181	2.14	20	1913	1097	21.69	36.18	14.49
	36-182	1.46	30	1864	847	22.34	43.35	21.01
	36-183	1.25	35.3	1882	757	22.10	46.56	24.46
	36-184	1.11	40	1858	669	22.42	50.15	27.73
	36-185	0.89	50	1975	570	20.90	54.92	34.02
	36-186	0.64	70	1943	380.6	21.30	67.50	46.19

Resistance measurements taken before and after exposure of the calorimeter to the electron beam (as described above) were used to calculate the difference in temperature ΔT induced by the radiation exposure. The relationship between temperature and radiation dose (reported by NPL from the alanine dosimeters) was defined by performing a regression of the ΔT data and the absorbed dose (as determined by the alanine dosimeters irradiated at the

same time as the calorimeters; the radiation received by the alanine dosimeters was measured by NPL so that the doses used for the calibration were traceable to a national standards dosimetry laboratory). Several polynomials (a linear equation, and 2nd, 3rd, 4th, and 5th degree polynomials) were fitted to the temperature and dosage data. The 2nd degree polynomial was found to have the lowest overall percentage error. Second degree polynomials of the general form

$$Y(\text{dose kGy}) = A + B(X) + C(X)^2$$

were found to give the best fitting to the data with the following constants:

Calorimeter	A	B	C
1095	0.0521	1.2621	0.0058
1096	0.0065	1.2631	0.0059.

After initial and final resistances were measured, the resistance values were entered into an Excel® spreadsheet and used to calculate the initial and final temperatures, and then the ΔT. From the ΔT value, using the equation and constants above, the radiation dose was calculated.

Using these constants, the following calculated ΔT values and radiation dosages are shown in Table 1 and Table 2 along with the dosages measured by the alanine reference dosimeters exposed at the same time. The absolute percentage errors are also given in Table 2.

TABLE 2

Alanine Reference #	ΔT (C) calorimeters		Absolute Dosage (NPL)	Calculated Dosage 2nd Degree Polynomial		Absolute % Error ±	
	1095	1096		1095	1096	1095	1096
36-177	0.58	0.52	0.353				
36-178	3.99	3.98	5.28	5.18	5.13	1.9	2.9
36-179	5.46	5.57	7.26	7.12	7.23	2.0	0.5
36-180	8.31	8.46	11.14	10.94	11.11	1.8	0.2
36-181	14.47	14.49	20.1	19.53	19.55	2.8	2.7
36-182	21.09	21.01	28.8	29.25	29.15	1.6	1.2
36-183	24.61	24.46	34.4	34.63	34.43	0.7	0.1
36-184	27.77	27.73	39.6	39.57	39.57	0.1	0.1
36-185	34.01	34.02	49.6	49.68	49.81	0.2	.04
36-186	46.35	46.19	71.1	71.01	70.94	0.1	0.2

In order to be meaningful, a dosage measurement should also be accompanied by an estimate of the uncertainty, as discussed in ASTM 1631. The measurement uncertainty was termed Total$_{ff}$ Uncertainty, and expressed as a percent. Total$_{ff}$ Uncertainty% was calculated from two underlying uncertainties, the uncertainty in the temperature measurement (due to the uncertainty in the correlation between thermistor resistance and temperature, and the component measurements) and the uncertainty in the radiation dosage measurement (due

to the uncertainty in the correlation between temperature change and radiation dosage, and the component measurements). The uncertainty in the measurement of temperature from thermistor resistance was termed $Total_{final}$ Uncertainty, and was expressed as a percentage. The uncertainty in the determination of dosage from the temperature change was termed $Dose_{max}$ Uncertainty and was determined by differences between the dose estimates calculated from the T-D data fitted to a 2nd degree polynomial compared to the absorbed dose measured using the NPL alanine dosimeters. The $Total_{ff}$ Uncertainty% was calculated by taking the square root of the sum of the squares of the underlying uncertainties $Total_{final}$ Uncertainty% and $Dose_{max}$ Uncertainty. These values are given in the following Table 3.

TABLE 3

$Total_{final}$ Uncertainty%		$Dose_{max}$ Uncertainty%		$Total_{ff}$ Uncertainty%	
1095	1096	1095	1096	1095	1096
± 2.58	± 2.42	± 2.84	± 2.90	± 4.12	± 4.10

The component uncertainties for the temperature measurement ($Total_{final}$ Uncertainty%) and dosage measurement ($Dose_{max}$ Uncertainty%) shown in Table 2 thus may be combined as the $Total_{ff}$ Uncertainty% and used to define the acceptance criteria for dosimetric release by calorimetry during routine production. The evaluation showed that the total uncertainty in this example was 4.1%.

Thus, the RISO calorimeters #1095 and #1096 were calibrated for use as routine dosimeters for monitoring the performance of an electron beam sterilization process utilizing the short, oval-shaped track conveyor of Example 1. Thermistor resistance measurements were used to determine temperature change and the ΔT was used to determine radiation dosage using the relationships and polynomial constants determined from fitting the measured ΔT and dosage calibration data. Resistance data from the thermistor calorimeter was recorded directly before entry of the calorimeter into the electron beam, and immediately after irradiation of the calorimeter. The raw resistance data was entered into a spreadsheet to accomplish two calculations. The first calculation translated the resistance data into temperature, and then the change in temperature from before to after the irradiation. The first calculation was accomplished by means of the relationship between resistance and temperature for the specific thermistor used in the measurement. The second calculation translated the change in temperature into a radiation dose. This translation of temperature change into dose was done using the relationship between the change in temperature and the radiation dosage obtained using alanine dosimeters obtained from, and evaluated by, NPL.

EXAMPLE 3

The method and system for routine dosimetry herein disclosed is suitable for use with other radiation processes. It has been integrated into the validated

SureTrack electron beam process control and record system (Titan Scan Systems, San Diego, CA) to accelerate production with fewer resources and far superior quality.

The SureTrack system prompts the operator to process a calorimeter at the appropriate frequency and automatically calculates the dose receive based on the resistance differential of the calorimeter. The dose values are then automatically recorded in the process report, providing an easy method to verify and document that the product received the proper dose.

Through the use of thermistor calorimetry as routine dosimeters in an electron beam sterilization process, the radiation dosage delivered during each processing run may be measured and recorded for process control, verification, and documentation. In such a report, such process details as identifying serial numbers of the calorimeters and other equipment used may be included, and details of the electron beam, including the process limits (low and high) for acceptable performance of the electron beam. For example, the beam current (typically in mA), power (typically kW), beam repetition rate (typically as pulses per second), scan magnet current (typically mA), scan magnet frequency (typically Hz), process rate (typically fpm), and the dosage delivered (typically kGy) are some important process parameters that may be included in a routine process report as part of the routine procedure in a radiation process.

The following is an example of such a process report used in the routine process, an E-Beam History Report.

Calorimeter ID	Resistance at Load	Resistance at Unload	Δtime
N1082-0010	1376 Ω	547 Ω	12 min
N1082-0004	2407 Ω	950Ω	11 min

	Low Limit	High Limit	First Pallet	Last Pallet
Ave. Beam Current (mA)	362	406	380	380
Klystron RF Ave. Power (kW)	3.85	4.14	4.00	4.07
Modulator Rep Rate (pulses/s)	190	210	200	200
Scan Magnet Current (mA)	50.2	55.4	52.0	52.0
Scan Magnet Frequency (Hz)	6.00	8.00	6.95	7.00
Process Rate (items/hour)	1.243	1.257	1.252	1.253
Dose (kGy)	20.0	50.00	36.66	33.67

The invention thus provides a fully integrated routine dosimetry system that is easy to use, requires minimal resources, provides complete documentation and minimizes quality and compliance issues.

It will be apparent from the foregoing that, while particular forms of the invention have been illustrated and described, various modifications can be made without departing from the spirit and scope of the invention. Moreover, those skilled in the art will recognize that features shown in one embodiment may be utilized in other embodiments.